UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/083,734	02/26/2002	David Needham	5405-212IPDV	3807

20792 7590 12/17/2003

MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

EXAMINER
KISHORE, GOLLAMUDI S

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/083,734	NEEDHAM, DAVID	
	Examiner	Art Unit	
	Gollamudi S Kishore, PhD	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-42 and 57-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-42 and 57-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims included in the prosecution are 38-42 and 57-65.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 38-42 and 57-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 38 recites an active agent besides a second component and a third component: Is the active agent in addition? Claim 38 does not use the term, 'first component', but uses the terms, 'second' and 'third'. What is the first component? Furthermore, line 5 recites 'material' in addition. What is this material? This terminology is confusing since according to the dependent claim 39, the material is the second component. The examiner suggests the naming of all the components in a Markush format.

'produced by another method' in claim 57 is not a positive expression; the examiner suggests naming of the methods.

The examiner also suggests defining 'surface active agent' in terms of specific compounds in claim 60 since phospholipid recited in the parent claim is also a surfactant (see also claim 63 which recites several phospholipids as surfactants).

It is unclear what applicant intends to convey by 'myristoyl, palmitoyl, stearoyl surfactants as recited in claim 61. This clarification is essential since the claim also recites palmitoyl , stearoyl alcohols. It is unclear is what applicant intends to convey by 'block copolymers'; block copolymers of what compounds? It is unclear what therapeutic lipids intend to convey. According to claim 57, the liposomes are already in a 'below the phase transition temperature'. Thus, it is unclear as to what applicants are intending to convey by 'a step of cooling the liposomes to a temperature below the phase transition temperature of the lipid bilayer prior to step a)'.

Claim Rejections - 35 U.S.C. § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 38-40, 42 and 65 are rejected under 35 U.S.C. 102(b) as being anticipated by Uster (4,828, 837).

Uster discloses liposomal compositions containing lysophosphatidic acid (second component) and phosphatidic acid (phospholipid) and the drug, minoxidil (third component) (note the abstract and examples, 10, 11 and 20 in particular).

5. Claims 38-40, 42 and 65 are rejected under 35 U.S.C. 102(b) as being anticipated by Radhakrishnan (4,906,476).

Radhakrishnan discloses liposomal formulations containing a lysolipid (second component) and a phospholipid for the delivery of steroids (third component) such as prednisone (note the abstract, columns 6-9, Example I on columns 15 and 16 and claims).

6. Claims 38-40, 42 and 65 are rejected under 35 U.S.C. 102(b) as being anticipated by DAUC (Jan. 1985).

DAUC discloses liposomal preparations containing phosphatidylcholine, ethanolamine, inositol, lysophosphatidylcholine (second component), lecithin, sugar lipids, surfactants and mixtures thereof. The method involves hydrating the lipid with an aqueous solution at a temperature higher than the phase transition temperature. The liposomes contain active agents such as antitumor agents, antibiotics, proteins, polysaccharides, vitamins and other medicinals (note the abstract).

7. Claims 38-40, 42 and 65 are rejected under 35 U.S.C. 102(b) as being anticipated by Ogawa (5,094,854)).

Ogawa discloses liposome compositions various drugs for hyperthermia therapy. The liposomes contain a mixture of lipids including the claimed combination and various drugs. (note the abstract, col. 1, line 58 through col. 4, line 37; Examples and claims).

8. Claims 38-40, 42 and 65 are rejected under 35 U.S.C. 102(b) as being anticipated by Eibl (5,626,867).

Eibl discloses liposomal formulations containing DPPC and DSPA (second component). The liposomes contain a variety of active agents including anti-tumor agents (note the abstract, col. 1, line 65 through col. 2, line 43, col. 4, line 39 through line 61; Examples, example 1 in particular and claims).

9. Claims 38-42 and 65 are rejected under 35 U.S.C. 102(b) as being anticipated by Alving (4,416,872).

Alving discloses liposomal formulations containing DPPC and a ceramide Second component. The liposomes contain a quinoline active agent. The method of preparation involves hydrating the lipid film with the aqueous medium. (Note abstract, Examples and claims).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 38-40, 42 and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hristova (Macromolecules, vol. 28, pp. 7693-7699, 1995)

Hristova discloses liposomal formulations containing dipalmitoylphosphatidylcholine and a lysolipid. The liposomes further comprise PEG derivatized lipids. Although Hristova does not teach instant lysolipid, monopalmitoylphosphatidylcholine, Hristova discusses the effect if lysolipids in general on gel phase bilayers and provides a specific example of the effect of the lysolipid, monooleoylphosphatidylcholine (note the abstract, Materials and Methods and Discussion). Therefore, it would have been obvious to one of ordinary skill in the art to use any lysophosphatidylcholine (that is substituted with any fatty acid moiety) with the expectation of obtaining similar effect on the gel phase bilayers. Hristova does not teach specific encapsulated active agents or a method of administration. However, in the introduction part, Hristova clearly suggests that the liposomes are for drug delivery and therefore, it would have been obvious to one of ordinary skill in the art to use the liposomes of Hristova for the drug delivery and hyperthermia therapy.

12. Claims 57-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uster or Radhakrishnan or DAUC or Ogawa or Eibl or Alving cited above, further in view of either Mayer et al (Chemistry and Physics of Lipids, vol. 40, pp. 333-345, 1986) or Boman et al (BBA, vol. 1152, pp. 253-258, 1993).

Uster, Radhakrishnan, DAUC, Ogawa, Eibl and Alving all teach classical metho of preparation of liposomes and not loading of drugs by a pH gradient.

Mayer et al disclose that loading of drugs into liposomes using pH gradients is advantageous since one can achieve trapping efficiencies approaching 100 %. The loading appears to be at room temperatures (note abstract).
Similarly Boman teaches increased trapping and retention of drugs such as vincristin using pH gradients. The temperature of loading is 37 degrees (abstract and Materials and Methods).

The use of pH gradient loading method for loading the drugs in the liposomes of Uster, Radhakrishnan, DAUC, Ogawa, Eibl or Alving would have been obvious to one of ordinary skill in the art since one can achieve higher trapping efficiencies as taught by Mayer et al or Boman et al.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 38-42 and 65 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S.

Patent No. 5,827,533. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant 'comprising' does not exclude cholesterol recited in the patented claims.

15. Claims 38-42 and 65 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 and 24 of U.S. Patent No. 6,200,598. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant generic claims include the specific components and the ratios recited in the claims of said patent.

16. Claims 38-42 and 65 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-31 of U.S. Patent No. 5,882,679. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant generic claims include the specific percentages of the lipid-polymr recited in the claims of said patent.

17. Claims 38-42 and 65 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,143,321. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant generic claims include the specific amounts of the surfactants in the patented claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, PhD whose telephone number is

703 308 2440. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703 308 2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1234.

Gollamudi S Kishore, PhD
Primary Examiner
Art Unit 1615

GSK